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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/786,839	03/01/2001	John R. White	P 50836	6619

20462 7590 11/19/2003

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EXAMINER

DELACROIX MUIRHEI, CYBILLE

ART UNIT	PAPER NUMBER
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1614

DATE MAILED: 11/19/2003

15

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/786,839

Applicant(s)

WHITE, JOHN R.

Examiner

Cybille Delacroix-Muirheid

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 September 2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-6 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,3,4 and 6 is/are rejected.
- 7) ☒ Claim(s) 2 and 5 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

Detailed Action

The following is responsive to Applicant's amendment received Sep. 5, 2003.

No claims are cancelled. No new claims are added. Claims 1-6 are currently pending.

Upon further reconsideration of the claims with a Primary Examiner, the following new ground of rejection is respectfully submitted.

Prosecution on the merits is re-opened. The allowability of claims 1-6 is withdrawn in view of the following new ground of rejection.

Claim Rejections - 35 USC § 112

1. Claims 1, 3, 4 and 6 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for N-[2-Hydroxy-4-cyanophenyl]-N'-[2-bromophenyl] urea and N-[2-Hydroxy-4-nitrophenyl]-N'-[2-bromophenyl] urea, does not reasonably provide enablement for all compounds which bind to the CXCR2 receptor or CXCR1 receptor and effectively inhibit T-cell mediated chemotaxis or block the binding of neutrophils to activated endothelial cells. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount

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of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The claims are drawn to a method of blocking the binding of neutrophils to activated endothelial cells or a method of inhibiting T-cell mediated chemotaxis by administering effective amounts of a compound which binds a CXCR2 receptor with claims 3 and 6 further requiring the administration of a compound, which binds to a CXCR1 receptor.

(2) The state of the prior art

The art recognizes the ability of a class of phenyl urea compounds to bind to CXCR2 receptors (a.k.a IL-8 β receptors) thus inhibiting the chemotaxis of neutrophils and T-cells. Such an inhibition is useful to treat a variety of diseases such as psoriasis, asthma, arthritis, etc. Please see the Widdowson reference, which is already made of record. Please also see the White et al. reference, which is also of record.

(3) The relative skill of those in the art

The relative skill of those in the art is high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical and chemical art is high.

(5) The breadth of the claims

The claims are very broad and encompass any compound, which would bind to a CXCR2 receptor or a CXCR1 receptor.

(6) The amount of direction or guidance presented

Applicant's specification provides guidance for and is only enabled for the use of N-[2-Hydroxy-4-cyanophenyl]-N'-[2-bromophenyl] urea and N-[2-Hydroxy-4-nitrophenyl]-N'-[2-bromophenyl] urea in the claimed methods. However, the specification provides no guidance to enable one of ordinary skill in the art to use the invention commensurate in scope with the claims, which, as stated above, are broad and encompass numerous compounds. In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result." Applicant's specification does not set forth a representative number of examples of compounds, which would bind to a CXCR2 or CXCR1 receptor and thereby block the binding of neutrophils to activated endothelial cells or inhibit T-cell mediated chemotaxis.

(7) The presence or absence of working examples

The examples in Applicant's specification provide working examples demonstrating the use of only two compounds, i.e. N-[2-Hydroxy-4-cyanophenyl]-N'-[2-bromophenyl] urea and N-[2-Hydroxy-4-nitrophenyl]-N'-[2-bromophenyl] urea for inhibiting neutrophil binding or T-cell mediated chemotaxis. Therefore, the specification

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enables one of ordinary skill in the art to use these two compounds in the claimed methods.

(8) The quantity of experimentation necessary

Since (1) the unpredictability of the chemical and pharmaceutical art is high, (2) chemical compounds differ radically in their properties, (3) Applicant's specification does not provide a representative number of compounds which would be capable of accomplishing the claimed methods, (4) the only working examples in the specification are directed to the use of two compounds in the claimed methods and (5) since compound structure and activity for pharmaceutical use must be determined from case to case by painstaking experimental study, one of ordinary skill in the art would be burdened with undue experimentation to determine all compounds which would bind to CXCR1 and CXCR2 receptors and which would be capable of inhibiting T-cell mediated chemotaxis or inhibit the binding of neutrophils to activated endothelial cells.

Claim Objections

2. Claim 2 is objected to because of the following informalities: in claim 2, line 3, "nitophenyl" should read –nitrophenyl--. Appropriate correction is required.

Specification

3. The incorporation of essential material in the specification by reference (please see page 5, lines 31-34) to a foreign application or patent, or to a publication (please see page 3, lines 12-19) is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing

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the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973). Please also see MPEP 608.01(p).

4. Claims 2 and 5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Claims 1, 3, 4, 6 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cybille Delacroix-Muirheid whose telephone number is 703-306-3227. The examiner can normally be reached on Mon-Fri. from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marianne Seidel, can be reached on (703) 308-4725. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

CDM



Nov. 15, 2003



**PHYLLIS SPIVACK
PRIMARY EXAMINER**